

Media Watch

SAMe targets consumers via the Web

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Touted as one of the most promising supplements ever introduced, *S*-adenosyl-L-methionine, or SAMe (pronounced “Sammy”), is found advertised on the Internet, in health and drug stores, and even in direct-to-consumer television ads since its introduction in the United States last year. Discovered in the 1950s, SAMe has been used widely in Europe for a variety of maladies, including depression, osteoarthritis, and liver disorders. This dietary supplement has been sought by US consumers primarily for its mood-enhancing effects.

Trials testing parenteral doses have shown SAMe to be effective for clinical depression

SAMe is a natural compound endogenously produced from adenosine triphosphate and the amino acid methionine. It then becomes a ubiquitous methyl donor to a wide variety of acceptor molecules and is involved in numerous metabolic pathways.¹ The exact mechanisms of action of SAMe for its purported health applications, principally as treatment of depression, are unknown. Limited animal and human data suggest that SAMe may play a role in alleviating depression by mechanisms such as modulating the monoaminergic systems and enhancing the neurotransmission resulting from the increase in neuronal membrane fluidity when modified by SAMe supplementation. The pro-

posed neuropharmacologic effects of SAMe on depression have been extensively reviewed by several authors.¹⁻³

Most early studies evaluating SAMe for depression were generally small and varied greatly in the patient population. A meta-analysis of selected clinical trials conducted for depression between 1973 and 1992 attempted to pool available data to assess the efficacy of SAMe compared with placebo (6 trials) and standard tricyclic antidepressants (7 trials). This study concluded that SAMe was more effective than placebo and comparably as effective as low to moderate dosages of tricyclic antidepressants.⁴ However, the substantial heterogeneity among these individual trials—patient populations, sample sizes, variable dosage regimens, and treatment durations—may limit the results found in this analysis. More recently, additional small double-blind trials have yielded positive results.^{5,6} Overall, trials testing parenteral doses have shown SAMe to be effective for clinical depression. Most trials have found the antidepressant effect to appear fairly rapidly (sometimes within 1 week) after the start of treatment. However, given the lack of large controlled trials and SAMe’s questionable oral bioavailability, more data are needed to support its use orally.

SAMe may be administered orally, intravenously, or intramuscularly, but only the oral formulation is commercially available in the United States. Most controlled studies of oral SAMe have employed a daily divided dose of 1,600 mg—but marketed supplements often recommend lower doses. Besides mild gastrointestinal distress, SAMe is generally well tolerated and does not appear to possess cardiac, anticholinergic, or orthostatic ef-

fects that may limit the clinical utility of many prescriptive antidepressants.^{7,8} Agitation and manic reactions have been reported to appear soon after SAMe administration.⁹⁻¹² For this reason, its use should be avoided in patients with a history of mania or

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bipolar disorders. There are no known confirmed drug interactions with SAMe. One case of serotonin syndrome in an elderly woman taking SAMe (intramuscularly) concurrently with clomipramine hydrochloride has been documented.¹³ The safety of concurrent use with the commonly prescribed selective serotonin reuptake inhibitors has not been evaluated. The coadministration of SAMe (intramuscularly) with imipramine hydrochloride (to hasten the onset of response to imipramine) did not reveal significant adverse effects.⁶

Consumers should be aware that the nutritional supplement industry is not well regulated and that the question of purity and potency remain. For instance, a company that conducts independent analyses of herbal, vitamin, and mineral supplements recently found disturbing discrepancies between the labeled amount and the actual amount of SAMe contained in various brand products selected for testing. Nearly half of the products evaluated did not pass testing.¹⁴ Consumers and clinicians should also consider the cost of therapy. The monthly cost of SAMe,

depending on the dose used, may be well over \$200, exceeding that of most prescription antidepressants.

The antidepressant potential of SAMe has generated much enthusiasm in this country lately, especially through the lay press. However, its claims of efficacy and safety for the treatment of depression need to be further justified through large controlled trials and by formal evaluation by the Food and Drug Administration. Follow-up studies to assess long-term tolerability and relapse rates are also needed.

At the time of this writing, Linda Shu was a 4th-year pharmacy student at the University of California, San Francisco, School of Pharmacy.

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Slides such as this one have appeared before feature films in some theatres in California. Sponsors hope young viewers get the message, which is designed to respond to the portrayal of tobacco use in movies as stylish and cool.

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